

Claims

1 1. A method for identifying phenotypes that vary in cell lines as a result of
2 genetic variation, comprising:

3 (a) measuring one or more phenotypes in cell lines from one or more pedigrees;
4 and

5 (b) testing whether the pattern of phenotype data in the cell lines conforms to the
6 rules of Mendelian transmission,

7 wherein conformation of said phenotype data to the rules of Mendelian transmission
8 is indicative that said phenotype varies in cell lines as a result of genetic variation.

1 2. A method for identifying phenotypes that vary in cell lines as a result of
2 genetic variation, comprising:

3 (a) measuring one or more phenotypes in cell lines from one or more pedigrees;
4 and

5 (b) testing whether the pattern of phenotype variation in the cell lines segregates
6 in the pedigree so as to produce a LOD score of at least 2 with one or more loci, and wherein
7 detection of a LOD score of at least 2 is indicative that said phenotype varies in cell lines as a
8 result of genetic variation.

1 3. The method of claim 1, wherein the phenotype is the mRNA level of a
2 selected gene.

1 4. The method of claim 2 where the LOD score is at least 3.

1 5. The method of any of claims 1 or 2, wherein the cell lines are derived from
2 the CEPH pedigrees.

1 6. The method of any of claims 1 or 2, wherein the gene or genes responsible for
2 the inter-cell line variation in phenotype are mapped to chromosomal loci by comparison of
3 the pattern of segregation of the phenotype in the cell lines with the pattern of segregation of
4 known mapped variances in the same cell lines.

1 7. The method of claim 4, wherein one or more candidate genes are evaluated by
2 determining if their chromosomal position is one of the chromosomal positions (loci) that
3 displays segregation with the phenotype.

1 8. The method of any of claims 1 or 2, wherein at least 15 cell lines from related
2 individuals are tested.

1 9. The method of any of claims 1 or 2, wherein the cells are subjected to a
2 treatment before measuring the phenotype, the treatment selected from the group consisting
3 of:

- 4 a. addition of a compound to the cells,
- 5 b. change in the nutritional environment of the cells, and
- 6 c. change in the physical environment of the cells.

1 10. A method for identifying mRNAs that vary in levels as a result of genetic
2 variation, comprising:

3 a. measuring levels of one or more specific mRNAs in cell lines from one or more
4 pedigrees; and

5 b. testing whether the mRNA levels of said one or more specific mRNAs in said cell
6 lines conforms to the rules of Mendelian transmission,
7 wherein conformation of any of said mRNA levels to the rules of Mendelian
8 transmission is indicative that said mRNA level varies in cell lines as a result of genetic
9 variation.

1 11. The method of claim 10, wherein said cell lines are derived from one or more
2 of the CEPH pedigrees.

1 12. The method of claim 10, wherein the gene or genes responsible for the
2 intersubject variation in levels of specific mRNAs are mapped to chromosomal loci by
3 comparison of the pattern of segregation of the mRNA levels in the cell lines with the pattern
4 of segregation of variances that are already mapped to the human genome.

1 13. The method of claim 10, wherein at least 100 cell lines from related
2 individuals are tested.

1 14. The method of claim 10, wherein said cells are subjected to a treatment before
2 performing the RNA analysis, the treatment selected from the group consisting of:
3 a. addition of a compound to the cells,
4 b. change in the nutritional environment of the cells, and
5 c. change in the physical environment of the cells.

1 15. A method for the identification of phenotypes that vary among cell lines as a
2 consequence of genetic variation, the method comprising:
3 a. Determining the genotype of a set of cell lines from unrelated subjects at candidate
4 genes for the phenotypes of interest;
5 b. measuring the phenotype in the cell lines; and
6 c. Measuring whether genetic variation among the cell lines correlates with variation
7 in the phenotype.

1 16. The method of claim 15 where at least 20 cell lines are analyzed.

USPTO-2025-01